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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,768	11/14/2000	Akira Asakura	20511/111693	9077

7590 05/07/2002

Mark E Waddell Esq
Bryan Cave LLP
245 Park Avenue
New York, NY 10167-0034

EXAMINER	
SLOBODYANSKY, ELIZABETH	

ART UNIT	PAPER NUMBER
1652	9

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/712,768	ASAKURA ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *1-21 and 51-56* is/are withdrawn from consideration.

5)☒ Claim(s) *22 and 23* is/are allowed.

6)☒ Claim(s) *25,26,28,29,31,33-40 and 42-45* is/are rejected.

7)☐ Claim(s) *24,27,30,32,41 and 46-50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The substitute specification filed February 26, 2002 has been entered.

Claims 1-56 are pending.

Election/Restriction

Applicant's election with traverse of Group II, claims 22-50, in Paper No. 7 filed February 26, 2002 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-21 and 50-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups I and III, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. 37 CFR 1.821(d) requires the use of assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences.

The following are examples of incompliance where sequence containing more than four amino acids or ten nucleotides are given without a sequence identifier: sequences shown at Figures 3-6 and 8 are not identified by sequence identifiers either in figures or in the description of Drawings.

Appropriate correction is required.

The specification is objected to because it is unclear what is intended to be indicated where "pH.45" is typed on page 9, clause (e).

Appropriate correction is required.

Claim Objections

Claims 24, 27, 30, 32, 41 and 46, with dependent claims 47-50, are objected to as dependent from claims 1-9 that are withdrawn.

Claims 24, 27, 30, 32, 41 and 46-50 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claims 37 and 45 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 37 and 45 recite a homolog of *Gluconobacter oxydans* DSM 4025, wherein said homolog is not included in the scope of the claims from which claims 37 and 45 depend.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25, 26, 28, 29, 31, with dependent claims 33-39, and claim 40, with dependent claims 42-45, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a DNA fragment encoding SEQ ID NO:4, 6 or 8, an expression vector and a recombinant microorganism comprising thereof. SEQ ID NO:4, 6 or 8 are 44, 38 and 29 amino acids in length and are encoded by SEQ ID NO: 3, 5 or 7, respectively. SEQ ID NO:4 is a fragment of cytochrome C II subunit (COII) and SEQ ID NOs: 6 and 8 are fragments of cytochrome C III subunit (COIII). The specification teaches that COII has molecular mass about 36 kD (page 3). From these and cloning data, it is apparent that the above sequences represent a small fragment of the corresponding full-length sequence (e.g., pages 28-29; Figure 7).

Thus, the claims are drawn to or depend from a genus of polynucleotides comprising a polynucleotide encoding SEQ ID NO:4, 6 or 8. The function of the encoded polypeptides is not limited. The specification does not contain any disclosure of the function of all DNA sequences comprising a polynucleotide encoding SEQ ID NO:4, 6 or 8. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs, both naturally occurring and man made, including partial DNA sequences, are encompassed within the scope of these claims. The above genus is functionally diverse as it encompasses polynucleotides encoding polypeptides having ability to form cytochrome C and those which lack such activity

but possibly have other undisclosed functions. The specification discloses only a single species of the claimed genus, SEQ ID NOs: 3, 5 and 7, and fails to provide any structure: function correlation present in all members of the claimed genus. As such, the disclosure of SEQ ID NOs: 3, 5 and 7 is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus that comprises the above sequences. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 25, 26, 28, 29, 31, with dependent claims 33-39, and claim 40, with dependent claims 42-45, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA fragment encoding SEQ ID NO: 4, 6 or 8, does not reasonably provide enablement for a DNA comprising DNA fragment encoding SEQ ID NO: 4, 6 or 8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the

art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

As discussed above, the claims are directed to a DNA encoding a polypeptide of any length having an undisclosed function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of encoded polypeptides having the ability to form cytochrome C and lacking said functions but possibly exhibiting other undisclosed functions.

With regard to polynucleotides encoding proteins retaining COII or COIII activity, the specification does not support the broad scope of the claims which encompass polynucleotides encoding polypeptides having amino acid sequence with low homology to the full-length amino acid sequence of COII or COIII. This is because the specification does **not** establish: (a) regions of the protein structure which may be modified without effecting the specific requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

With regard to polynucleotides comprising polynucleotides encoding polypeptides of SEQ ID NO: 4, 6 or 8 and having no known function, the specification does not provide a guidance as to how to use said polynucleotides. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which structure would impart the desired activity requires a detailed knowledge of the ways in which the proteins' structure relates to its function and vice versa. In general, the state of the art does not allow the predictability of function based on structure. The disclosure lacks any information regarding the correlation between

function and structure. Without knowing the function it is impossible to know how to use a DNA fragment.

Thus, one of ordinary skill in the art would require guidance, in order to make a DNA fragment encoding a polypeptide retaining COII or COIII function and having any structure comprising SEQ ID NO: 4, 6 or 8, in a manner reasonably correlated with the scope of the claims.

Furthermore, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a DNA fragment that comprises a DNA encoding SEQ ID NO:4, 6 or 8 and encodes a polypeptide of any undisclosed function. Without such guidance, the experimentation left to those skilled in the art is undue.

Claims 36 and 44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that *Gluconobacter oxydans* DSM 4025 is required to practice the claimed invention. As a required element it/they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it/they

is/are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the microorganism(s). See 37 C.F.R. § 1.802.

The specification does not provide a repeatable process for obtaining the microorganism(s) and it is not apparent if the microorganism(s) is/are readily available to the public. The specification must contain the date that the microorganism(s) was/were deposited, the name of the microorganism(s) and the address of where the microorganism(s) was/were deposited.

Since the deposit(s) has/have been made under the terms of the Budapest Treaty (page 18), an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his/her signature, and registration number, stating that the specific strain(s) has/have been deposited under the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37, 44 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37 and 45 recite the term "a biological or taxonomic homolog of a microorganism having the identifying characteristics of *Gluconobacter oxydans* DSM 4025". The metes and bounds of said term are unascertainable. The term "homolog" is not clearly defined in the art. The specification refers to the term on several occasions, but the term is not specifically defined. Furthermore, the difference between "a biological homolog" and "a taxonomic homolog" is unclear. The lack of the clear definition of the scope of the term renders claims 37 and 45 indefinite.

Claim 44 is confusing because it is directed to "a recombinant microorganism" whereas *Gluconobacter oxydans* DSM 4025 is not a recombinant microorganism.

Allowable Subject Matter

Claims 22 and 23 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

May 3, 2002